81. (Amended) An isolated, antigenically reactive HAV peptide, the antigenically reactive peptide comprising an amino acid sequence of a portion of the P2A protein of HAV corresponding to amino acids 792 to 980 and to a portion of an HAV protein selected from the group consisting of the VP3 protein of HAV corresponding to amino acids 246 to 491; the VP1 protein of HAV corresponding to amino acids 492 to 791; the P2A protein of HAV corresponding to amino acids 792 to 980; the P2B protein of HAV corresponding to amino acids 981 to 1087; the P2C protein of HAV corresponding to amino acids 1088 to 1422; the P3A protein of HAV corresponding to amino acids 1423 to 1496; the P3B protein of HAV corresponding to amino acids 1497 to 1519; the P3C protein of HAV corresponding to amino acids 1520 to 1738; and conservative variations thereof, wherein the antigenically reactive HAV peptide is not identical to a HAV polyprotein , wherein the amino acid sequence of at least a first portion of P2A sequence and a second portion of P2A sequence are switched in order with one another relative to the amino acid sequence of wild-type HAV P2 protein and wherein the antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS: 38, 42 - 46 and conservative variations thereof.

REMARKS

Claims 70-72 and 77-82 were pending in this application after entry of newly submitted claims 79-82 by the Examiner. However, as noted by the Examiner, claims 79-82 are alleged to be directed to an invention that is either independent or distinct from the invention originally claimed and, consequently, claims 79-82 have been withdrawn from consideration by the Examiner. Thus, claims 70-72 and 77-78 are under examination on the merits.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page showing changes to the claims is captioned "Version with markings to show changes made." No new matter is believed added. Support for these amendments can be found throughout the specification, as set forth below.

Specifically, support for the amendment of claims 70-71, 77, 79 and 81 to recite "...consisting of SEQ ID NOS:38, 42-46" can be found, for example, on page 4, line 1 to page 5, line 26, wherein is recited "...peptide selected from the group consisting of..." followed by listings of appropriate SEQ ID NOS. As selected from indicates also that some can omitted from a selection, Applicants submit that the present recitation of sequences is fully supported by the specification as filed. Support for the amendment of claim 79 to recite "....wherein at least one HAV protein selected is the P2A protein..." is evident from throughout the specification and claims as filed. Support for amendment of claim 81 to recite "...wherein the amino acid sequence of at least a first portion of P2A sequence and a second portion of P2A sequence are switched in order with one another relative to the amino acid sequence of wild-type HAV P2 protein..." can be found in the specification at page 25, lines 3-21, wherein mosaic proteins formed by fusion of more than one immunogenic peptide together in a single polypeptide and in the recognition, as evidenced also at page 24, lines 15-21, that the immunogenic peptides need not be placed in specific order or be contiguous one with another for the present invention to be operative.

In light of the following remarks, Applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

Applicants traverse the Examiner's determination that claims 81-82 are drawn to species which were nonelected without traverse in Paper #16. Applicants did elect a single species corresponding to the P2A protein. That species is embodied in the claim 81 as it recites, "... the antigenically reactive peptide comprising an amino acid sequence of a portion of the P2A protein of HAV..." While there can be other amino acids present in the peptide, the claim clearly does encompass the elected species and, if a peptide does not include the elected species, it would not be covered by claim 81 or claim 82 dependent thereon. In addition, Applicants have amended claim 79 to explicitly recite that the elected species, those including sequence corresponding to the P2A protein, be included. Accordingly, Applicants respectfully request that claims 81-82 and claims 79-80, as amended, be examined as they do recite the elected invention.

I. Objections

Applicants acknowledge withdrawal of rejection to the specification.

In response to the alleged informalities of claim 72 and 78, Applicants submit that claim 72 is not missing an article "the" in the second from last line. Use of an article "the" is not appropriate as "the sequence" would necessarily refer to an earlier antecedent "sequence." As the first recited "sequence" indicates sequence included in the antigenically reactive peptide and the second "sequence" indicates sequence that is excluded from the antigenically reactive peptide, altering the claim as suggested by the Examiner would alter the meaning and clarity of the claim.

Similarly, the objection to claim 78 for allegedly missing either an article or a phrase from line 2 between "of" and "sequence" is inappropriate. The sequence referred to by "of sequence" is not limited to the particular sequences identified as SEQ ID NOS:38-43, but rather refers to sequence more generically which is defined by SEQ ID NOS:38-43. Correspondingly, claim 78 recites a peptide having no sequence corresponding to sequence defined by SEQ ID NOS:38-43.

II. Rejection under 35 U.S.C. § 112, second paragraph

A. Previous Grounds of Rejection

Claims 70-72 and 77-78 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly not particularly pointing out and distinctly claiming the subject matter which the Applicants regard as their invention.

Applicants acknowledge withdrawal of the rejection of claims 70-72 for use of "substantially similar" language.

Rejection of claim 70 and claims dependent thereon and of new claims for use of term "portion" has been maintained by the Examiner. Specifically, the Examiner has stated that the present claims encompass any and all antigenically reactive HAV peptides which comprise any portion of the P2A protein of HAV as a "portion" has been defined as "any fraction up to and including the complete item." Consequently, the Examiner alleges that the claims would encompass virtually all antigenically reactive peptides because each would likely share at least one amino acid in common with the recited P2A protein.

Applicants submit that the claims that include a clause that requires that "...the antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS:38-46 and conservative variations thereof," renders the claims definite. As the claims require that the antigenically reactive HAV peptide of the claimed invention, which must include P2A sequence, be capable of binding with an antibody specifically antigenically reactive with peptides derived from P2A sequence, the claims cannot be construed to encompass all antigenically reactive HAV peptides. Thus, when read and considered in their entirety, the present claims are not indefinite as is alleged by the Examiner. Furthermore, Applicants submit that it is well-established that the "[d]efiniteness of claim language must be analyzed, not in vacuum, but in light of...the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made" (MPEP 2173.02). As it is understood by all skilled practitioners of the pertinent art, an "antigenically reactive peptide" that binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS:38-46 and conservative variations thereof, does not encompass all antigenically reactive HAV peptides as is alleged by the Examiner, but would rather be considered by those of skill in the art to encompass a smaller set of peptides defined both in terms of structure and function, albeit not without a degree of flexibility in the exact structure contemplated. Accordingly, Applicants request removal of this basis of rejection.

Applicants acknowledge Examiner's withdrawal of the rejection of claims 70-72 for use of phrase "conservative variations."

The Examiner maintains that the claims are indefinite due to the lack of a specific reference sequence upon which the claims are based. Further, the Examiner indicates that in the absence of such a definition, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

In response, Applicants refer the Examiner to § 2173.02 of the MPEP wherein it is clearly stated that compliance with the requirement for definiteness of 35 U.S.C. § 112, 2nd para, is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or expression are available. As outlined therein, section 2173.02 further states that definiteness is to be determined, "...not in a vacuum, but in light of: (a) [t]he content of the particular application disclosure; (b) [t]he teachings of the prior art; and (c) [t]he claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." In the present instance, these teachings within the application itself to be considered include; that the HAV polyprotein is expressed as "a single polyprotein that is subsequently processed into structural and nonstructural proteins" (page 1, lines 18-19), that the particular regions named correspond to particular amino acid residues of the polyprotein (see headings to each of Tables 2-11); that the numbering of amino acid residues of contiguous protein domains, e.g. SEQ ID NOS:28 and 29, wherein there is a 13-residue overlap that corresponds to an overlap of 13 residues indicated by the "localization aa" in the table; and that the present application teaches that the amino acids making up a peptide, i.e., amino acid residues, "...are numbered in order, starting at the amino terminal and increasing in the direction of the carboxy terminal of the

peptide" (page 11, lines 35-36). Each of these indicate that the present specification describes the whole polyprotein that is expressed in terms of amino acid residues and numbering thereof based upon the originally expressed, intact polyprotein. Similarly, the teachings of the prior art that are also to be considered, as outlined by the MPEP, include reference to and use of the same numbering system to identify regions and/or residues of HAV proteins. Specifically, Applicants refer the Examiner to Chiron (0 199 480), column 2, lines 19-26, wherein a systematic nomenclature convention is described and to lines 34-36 wherein it is stated that "[a]s shown by the invention herein, this pattern is consistent for HAV encoded polypeptides as well." Finally, in respect to the teaching of Chiron, Applicants note that the Examiner rejected claims 70-72 under 35 U.S.C. § 103(a) as being unpatentable over Chiron because it teaches, *inter alia*, a preferred immunogenic peptide as derived from AA 792-848 (in claim 14 of Chiron) that the Examiner alleges corresponds to peptides comprising an amino acid sequence corresponding to AA 792-980 (the P2A protein of the present application) (see page 5 of Paper 22 issued May 15, 2001). While perhaps not surprising given that the two numbering systems are identical, the Examiner apparently had no difficulty in identifying these corresponding regions in the present application and in Chiron, known art in the field that antedates the present application. Indeed, while rejecting the present claims for indefiniteness because they allegedly are not clear as to what sequence "amino acids 792 to about 980" are referring, the Examiner also specifically cites a sequence drawn from the prior art, specifically Chiron, that uses the same numbering system and describes a P2A protein derived from AA 792-848. The sequence nomenclature of the present application is not only adequate for the Examiner to identify that there is some correspondence between them, it is such that the amino acid

residue numbering of one, as judged by the start of the P2A protein, matches the amino acid residue numbering of the other for the same protein. Surely then the presently used numbering system and nomenclature are not indefinite when the criteria laid out in making such a determination are properly considered, as in addition to the above-indicated contents of the specification and teachings of the prior art, "the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made" is also to be considered. As this "claim interpretation" has already been properly indicated without explicit admission by the Examiner as referring to the same numbering system known in the art, Applicants submit the Examiner's rejection on this basis is most unjustified and improper. Applicants therefore request its withdrawal.

However, as the Examiner states that the "applicant's arguments have been fully considered but they are not persuasive because they do not define a *specific reference sequence* upon which the claims are based" and that "[a]bsent such definition, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite" (emphasis added), Applicants believe the Examiner's position may be more consistent with rejection under other sections of the code than with 35 U.S.C. § 112, 2nd para. Particularly, if the Examiner believes that the present claims are unduly broad because they are not supported by an enabling disclosure, Applicants submit that the Examiner address that concern under 35 U.S.C. § 112, 1st paragraph, in a new non-final rejection. Alternatively, if the Examiner believes that the present claims are so broad that they read on the prior art or are obvious in light of the prior art, Applicants submit that the Examiner address those concerns under 35 U.S.C. §§ 102 or 103 in a new non-final rejection. Applicants request

consideration of these points by the Examiner so that the rejection of the claims by the Examiner be properly presented so that the prosecution record presents the merits of the relative positions with clarity and precision.

B. New Grounds of Rejection

Claim 71 is rejected as indefinite for use of the phrase "can include." Applicants have amended claim 71 to recite "includes" thereby eliminating this basis for rejection.

Claim 71 is also rejected for use of the term "small" as the Examiner alleges that this term, because it is relative, renders the claim indefinite. Applicants submit that the term does not render the claim indefinite as its meaning within the phrase "small percentage of amino acids," is defined in the specification. Specifically, on page 13, lines 16-17, it states "...small percentage of amino acids (typically less than 5%, more typically less than 1%)..."

Claim 72 is rejected as indefinite as the limitation "wherein ... at least one of SEQ ID NOS:38-43 is excluded..." is alleged to exclude the same sequence that are specifically recited in the base claim. Applicants respectfully disagree. The base claim, directed to peptides including sequence corresponding to protein P2A (i.e., sequence corresponding to SEQ ID NOS:38-46), need not include sequence corresponding to all of SEQ ID NOS:38-43. Consequently, a peptide can both include sequence selected from SEQ ID NOS:38-46; for example, SEQ ID NOS:38-39; and exclude sequence selected from SEQ ID NOS:38-43; for example, SEQ ID NOS:40-41. As discussed *supra* in regard to the objection of claim 72 for lack of the article "the," the earlier recited sequence included is not the antecedent for sequence that is excluded.

Similarly, claim 78 is rejected for indefiniteness as it is unclear whether the claim is intended to exclude portions or all of SEQ ID NOS:38-43. As indicated in the response to the objection to this claim for allegedly missing either an article or a phrase from line 2 between "of" and "sequence," there is no missing article. The sequence referred to by "of sequence" is not limited to the particular sequences identified as SEQ ID NOS:38-43, but rather refers to sequence more generically which is defined by SEQ ID NOS:38-43. Correspondingly, claim 78 recites a peptide having no sequence corresponding to sequence defined by SEQ ID NOS:38-43. Such a peptide could include sequence from SEQ ID NOS:44-46.

Applicants submit that the presently amended claims do fulfill all requirements as outlined under 35 U.S.C. §112, second paragraph, and request, therefore, removal of this basis of rejection.

III. Rejection under 35 U.S.C. § 112, first paragraph

Claim 72 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that amendment of claim 72 to recite "wherein the amino acid sequence from at least one of SEQ ID NOS:38-43 is excluded" is not supported by the disclosure as originally filed.

Applicants submit that the amendment of claim 72 is supported by the specification as filed. Applicants would draw the Examiner's attention to p. 25, lines 4-5 of the specification wherein it states "[t]ypically, 2 to 20 of the immunogenic peptides are fused into a single polypeptide..." As no

two (2) peptides that can be selected from the group consisting of SEQ ID NOS:38-43 can define all of the sequence defined by the complete group, amendment to recite "wherein amino acid sequence from at least one of SEQ ID NOS:38-43 is excluded" is clearly supported by the disclosure as originally filed. Applicants would also emphasize that the claim, as amended, recites "..wherein amino acid...", not "wherein, the amino acid..." and refer the Examiner to the comments regarding objections to claim 72. Support for this amendment can also be found on page 4, line 1 to page 5, line 26 and in Tables 4 and 5 where SEQ ID NOS:38-46 are described as examples of peptides that can define the antigenic peptide. Thus, Applicants adequately describe and support each of SEQ ID NOS:38-43. Therefore, by amending the claim to include a limitation that a peptide of one or more of these SEQ ID NOS is excluded from the claimed polypeptide, Applicants are merely claiming less than the full scope of their disclosure, which has precedent in the patent case law. See e.g., *In re Johnson and Farnham*, 558 F.2d 1008, 194 USPQ 187 (CCPA 1977). Thus, Applicants believe this rejection has been overcome. Applicants request removal of this basis of rejection and the proper consideration of the corresponding amendment to claim 72.

IV. Rejection under 35 U.S.C. § 103

The rejection of claims 70-72 under 35 U.S.C. § 103(a) as unpatentable over Chiron is maintained. Newly added claims 77-78 are also rejected under 35 U.S.C. § 103(a) as being unpatentable over Chiron Corporation for the reasons of record. Specifically, the Examiners states that: 1) the Applicants' argument that Chiron neither made nor tested any peptide corresponding to AA 792-848 has been previously addressed; and 2) Applicants' proposed claim amendments to

eliminate the "substantially similar" language would not distinguish over Chiron because the proposed claims are drawn to an antigenically reactive HAV peptide comprising an amino acid sequence of a portion of the P2A protein. The Examiner then states that because of the reasons set forth *supra,* the Applicant's claims are not drawn exclusively to a peptide corresponding to AA 792-848.

In response, Applicants' submit that the previous amendment of the claims does distinguish the present claimed invention over Chiron. Specifically, Applicants refer to the previous amendment of claims 70-71, 77, 79 and 81 to limit the antigenically reactive peptide of the invention to those that bind to an antibody specifically antigenically reactive with peptides selected from the group consisting of SEQ ID NOS: 38 - 46 and, except in the case of claim 71, conservative variations thereof. As this language does clearly limit the claims to those peptides of the invention that include sequence from a portion of the P2A protein (i.e., AA792-848), rejection of these claims over teachings of binding to antibodies that are cross-reactive with peptides derived from other sequences that fall outside the range of sequence defined by SEQ ID NOS:38-43 is inappropriate.

In regard to the Examiner's comments concerning Applicants' arguments that Chiron was wrong (1st full paragraph on page 6 of Paper 31), Applicant submits that, as stated, the Office Action misrepresents the teachings present in Exhibits A-D. In particular, the Examiner states that "...each of the articles explicitly teaches that the nonstructural proteins are indeed antigenically reactive in immunoassays and also are immunogenic." This is not entirely accurate, nor is it particularly relevant. As the Examiner notes, in both Exhibit B and Exhibit C, Robertson et al. teach that P2 antibodies do develop in humans and in chimpanzees following infection by the *complete virus*

(emphasis added). However, that is no indication that an isolated protein or a fragment of protein is adequate to cause the same effect. Indeed, the cited portion of Jia et al. (Exhibit D), wherein it states that "infected individuals had antibodies that recognized uncleaved P1 proteins as well as nonstructural antibodies," teaches only that intact nonstructural proteins are antigenically reactive, not that they are immunogenic. Further, the antigenic reactivity of an intact nonstructural does not necessarily indicate that fragments of that protein are or are not antigenic. Thus, even if only considering the portions of the references cited in support of a rejection for obviousness, there is not adequate support for such a finding of obviousness over all the claims. Namely, application of teachings regarding the antigenic reactivity of intact proteins of wild-type sequence to polypeptides that comprise less than the complete protein, as is the case in claims 77-80, or where the order of particular elements of sequence are altered, as is the case in claims 81-82, do not support a finding of obviousness.

Indeed, in Jia et al., there is an explicit teaching that teaches against the use of fragments of P2A. As shown in Figure 2.B (page 277 of Exhibit D), immunoprecipitation of P2 protein is entirely abolished by denaturation. Further, on page 279, the first column, Jia et al. state "[i]n each case, heat denaturation of the antigens in the presence of SDS before immunoprecipitation led to loss of antigen reactivity, suggesting that these antigens contain *conformation-specific dependent or noncontiguous epitopes* that are sensitive to denaturation" (emphasis added). Thus, the prior art taught that use of fragments that are inadequate to support the conformation of the protein, could not be expected to provide an antigenically reactive peptide, i.e., reactivity is conformation-specific dependent. Further, the authors interpreted this result to indicate that the antigens contained

noncontiguous epitopes. Correspondingly, one of skill in the art would not be motivated to produce the present invention. As the peptide of claims 77-80 must necessarily lack a portion of P2A, there can be no expectation that the peptide would be antigenically reactive. Further, as the order of noncontiguous epitopes would be considered by one of skill in the art to effect the folding and overall conformation of the protein, any peptide of the invention that alters the natural order of sequences, such as required in claims 81-82, following amendment of claim 81, would also provide no reasonable expectation of success.

As no representation by the Examiner of the cited art (Exhibits B-D) properly teaches the antigenic reactivity of fragments of the P2A protein, and explicit teachings in this art indicate that fragments or proteins with modified sequence would not be antigenically reactive, Applicants submit that there is no proper basis for a finding of obviousness that relies on this art. Indeed, Applicants submit that this art teaches against the present invention even when combined with Chiron et al.

Chiron is characterized by the Examiner to specifically teach individual peptides corresponding to portions of the P2A protein. This position is alleged to find support in Chiron at page 3, column 3, lines 2-48. However, the Office Action only quotes from lines 44-48, where it states "...polypeptides which may serve either as vaccines themselves, or as intermediates in the production of monoclonal antibody (Mab) preparations useful...as diagnostic reagents." Consideration of a further portion of this same text, lines 19-28, provides a significant change in meaning as when referring to previously-determined partial sequences of the HAV polyprotein, it states "[t]hese reports have yielded insufficient information to permit construction of polypeptides

which can serve as vaccines. The present invention provides the entire genomic sequence of HAV, and thus permits manipulation of the potential epitopes to obtain effective vaccines against HAV." As the earlier partial sequences provided at least a portion of the polyprotein sequence, Chiron itself teaches that not all fragments of the polyprotein are adequate to produce a vaccine. Indeed, this portion only states that the entire genomic sequence provided "*permits manipulation of potential epitopes*" (emphasis added). Further, in lines 37-41, the invention of Chiron is stated to provide "...the entire viral polypeptide sequence and *permits* not only analysis, but *production of portions* thereof, *if appropriate*, in the correct configuration, so as to provide effective vaccines..." (emphasis added). Like the earlier quoted portion, this section of Chiron also does not state which portions should be used; however, more importantly, it does not even maintain that use of a portion is appropriate. Thus, while claim 14 of Chiron does recite a particular P2A epitope, derived from amino acids 792-848 of the HAV polypeptide sequence, and Chiron does provide the complete sequence of HAV, it does not provide any other portion of P2A for use as an antigen. Further, even that portion of P2A that is provided is not confirmed to be an appropriate polypeptide antigen.

Coupled with Jia et al. that teaches against the use of fragments of P2, Chiron's teaching that the complete sequence permits "...production of portions thereof, if appropriate,...to provide effective vaccines..." is not an adequate basis for a finding of obviousness for any claim of the present application, but particularly it is not adequate for claims 77-82 that exclude the sequence from claim 14 in Chiron as recited. In particular, claims 77-80 must necessarily lack a portion of the recited sequence and claim 81 as amended, and claim 82 dependent thereon, can only include the complete sequence in an altered form where the order is no longer that described by Chiron.

Any such modification of the sequence provided in Chiron is neither taught nor suggested by either Chiron or the other references discussed or any combination of Chiron with those references. As discussed in the MPEP § 2143, two of the three basic requirements of a *prima facie* case of obviousness are that there must be suggestion or motivation in the references themselves, or in the knowledge available to one of ordinary skill in the art to modify the reference, and that the prior art teaching must teach or suggest all the claim limitations. As is explained herein, Chiron does not provide suggestion or motivation as it explicitly indicates that fragments can be made when appropriate, but does not indicate any fragments of the P2A protein, other than that described in claim 14 of Chiron. Further, the knowledge available to those of skill in the art did not teach or suggest the claim limitations, but rather taught against the invention as there could be no expectation of success in light of the teaching of Jiang et al.

Applicants request that the Examiner not be influenced by earlier determinations of obviousness, but that the determination be made on the basis of all the evidence presently before the Examiner. Specifically, Applicants request that all the teachings of Chiron, Robertson et al. and Jia et al. be taken into account for what they teach, as properly described herein, instead of relying on only portions of some of these references, as was used earlier to establish the Examiner's case for obviousness. Moreover, Applicants also request that the Examiner take into account the teachings of the provided Exhibits A-D which, when properly read, interpreted and applied, do not teach the obviousness of the present invention as is alleged by the Examiner, but instead strongly teach against a determination of obviousness and, as such, do not support rejection of the present claims. Applicants therefore request removal of this basis of rejection.

Finally, in regard to the Examiner's statements in the last paragraph of the section outlining the rejection under 35 U.S.C. § 103; Applicants submit the Examiner has not fully considered the Applicants arguments. Specifically, Applicants refer to the Examiner's comments that the Applicant's arguments that "no peptide claimed by any new claim corresponds to the portion of the P2A protein disclosed in Chiron is not understood, as the newly added claims also recite the P2A protein of HAV corresponding to AA 792-980, as is recited in the originally presented claims."

In response, Applicants reiterate what was stated in the last response; specifically, that in each of the newly added claims (i.e., claims 77-82), there is a limitation or modification to the sequence of the claimed peptide that distinguishes it from that disclosed in Chiron. Specifically, the peptide of claim 77 must not contain the complete sequence of the portion of the P2A protein disclosed in Chiron as it recites "... the antigenically reactive peptide lacks a portion of sequence selected from the group consisting of SEQ ID NOS:38-43." The peptide of claim 78 must not contain any portion of the portion of the sequence of the specific P2A protein disclosed in Chiron, i.e., the disclosed peptide of claim 14 in Chiron that recites amino acids 792-848. Specifically, the peptide of claim 78 excludes sequence from that specific region of sequence as it recites "...wherein the peptide contains no portion of sequence selected from the group consisting of SEQ ID NOS:38-43." The peptide of claim 79 must include additional sequence from at least one other HAV protein not disclosed in the portion of the P2A protein disclosed in Chiron as it recites "...comprising an amino acid sequence of only a portion of at least two HAV proteins." The peptide of claim 80, dependent from claim 79, must also include sequence not contained in any HAV polyprotein as it recites "...wherein the sequence of the antigenically reactive HAV peptide is not contained in any

HAV polyprotein." The peptides of claims 81 and 82 must include both at least a portion of the P2A protein, including that supposedly disclosed in Chiron, and portions of further proteins of the HAV polyproteins, wherein sequence included in the peptides of claims 81 and 82 are not contained in any HAV polyprotein.

As described above and in the claims, when read in full claims 77-82 necessarily differ from that of the specific P2A described in Chiron. Further, as there is no teaching or suggestion in Chiron to make these necessary modifications to the sequences disclosed in Chiron, or the sequence of the full-length HAV polyprotein, Chiron fails to render the invention as claimed obvious. Applicants request removal of this basis of rejection.

V. Rejection under 35 U.S.C. § 102

Claims 70-72 and 77-78 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Robertson et al. Specifically, certain sequences cited are alleged to anticipate the claimed invention as described by the Examiner to be, "an isolated antigenically reactive HAV peptide comprising a portion of the amino acid sequence of the P2A protein of HAV corresponding to amino acids (aa) 792-980,...corresponding to a portion or all of an amino acid sequence selected from SEQ ID NOs:39-46." More specifically, the Examiner alleges that Robertson et al. teaches a fragment which comprises SEQ ID NO:39 (see Accession No.PQ0431), a fragment which comprises SEQ ID NO:40 and the first 10 amino acids of SEQ ID NO:41 (see Accession No.PQ0433), and other fragments the first 10 amino acids of SEQ ID NO:41 (see Accession Nos.PQ0434, PQ0428, PQ0427, PQ0429, and PQ0430).

In response, Applicants submit that the amendment of each of the presently pending claims to require that the "antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS:38, 42-46" and, in some cases, "conservative variations thereof" render the rejection by the Examiner over Robertson et al. moot as each of the sequences cited by the Examiner as being anticipated by Robertson et al. has been removed. Correspondingly, each claim now must necessarily include binding to antibodies specific for peptides outside of those cited by the Examiner. Accordingly, Applicants request withdrawal of this basis of rejection and allowance of these claims to issue.

Pursuant to the above amendments and remarks, consideration and allowance of the pending application is believed warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

Credit Card Form PTO-2038 authorizing payment in the amount of $400.00 (two-month extension of time fee) is enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required to Deposit Account No. 14-062.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date shown below.

Gwendolyn D. Spratt

Gwendolyn D. Spratt

Date

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

70. (Thrice amended) An isolated, antigenically reactive hepatitis A virus (HAV) peptide, the antigenically reactive peptide comprising an amino acid sequence of a portion of an HAV protein selected from the group consisting of the VP3 protein of HAV corresponding to amino acids 246 to 491; the VP1 protein of HAV corresponding to amino acids 492 to 791; the P2A protein of HAV corresponding to amino acids 792 to 980; the P2B protein of HAV corresponding to amino acids 981 to 1087; the P2C protein of HAV corresponding to amino acids 1088 to 1422; the P3A protein of HAV corresponding to amino acids 1423 to 1496; the P3B protein of HAV corresponding to amino acids 1497 to 1519; the P3C protein of HAV corresponding to amino acids 1520 to 1738; and conservative variations thereof, wherein the antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS: 38, 42 - 46 [11-72] and conservative variations thereof.

71. (Thrice amended) The antigenically reactive peptide of claim 70, wherein the amino acid sequence includes [can include] individual substitutions, deletions or additions which alter, add or delete a single amino acid or a small percentage of amino acids, and wherein the antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS: 38 and 42 - 46 [11-72].

77. (Amended) An isolated, antigenically reactive HAV peptide, the antigenically reactive peptide comprising an amino acid sequence of a portion of an HAV protein selected from the group consisting of the VP3 protein of HAV corresponding to amino acids 246 to 491; the VP1 protein of HAV corresponding to amino acids 492 to 791; the P2A protein of HAV corresponding to amino acids 792 to 980; the P2B protein of HAV corresponding to amino acids 981 to 1087; the P2C protein of HAV corresponding to amino acids 1088 to 1422; the P3A protein of HAV corresponding to amino acids 1423 to 1496; the P3B protein of HAV corresponding to amino acids 1497 to 1519; the P3C protein of HAV corresponding to amino acids 1520 to 1738, wherein the antigenically reactive peptide lacks a portion of sequence selected from the group consisting of SEQ ID NOS:38-43, and wherein the antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS: 38, 42- 46 [11-72] and conservative variations thereof.

79. (Amended) An isolated, antigenically reactive HAV peptide, the antigenically reactive peptide comprising an amino acid sequence of only a portion of at least two HAV proteins selected from the group consisting of the VP3 protein of HAV corresponding to amino acids 246 to 491; the VP1 protein of HAV corresponding to amino acids 492 to 791; the P2A protein of HAV corresponding to amino acids 792 to 980; the P2B protein of HAV corresponding to amino acids 981 to 1087; the P2C protein of HAV corresponding to amino acids 1088 to 1422; the P3A protein of HAV corresponding to amino acids 1423 to 1496; the P3B protein of HAV corresponding to amino acids 1497 to 1519; and the P3C protein of HAV corresponding to amino acids 1520 to 1738, wherein the

antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS: 38, 42 - 46 [11-72] and conservative variations thereof , wherein at least one HAV protein selected is the P2A protein and wherein the antigenically reactive peptide is not a full-length HAV polyprotein.

81. (Amended) An isolated, antigenically reactive HAV peptide, the antigenically reactive peptide comprising an amino acid sequence of a portion of the P2A protein of HAV corresponding to amino acids 792 to 980 and to a portion of an HAV protein selected from the group consisting of the VP3 protein of HAV corresponding to amino acids 246 to 491; the VP1 protein of HAV corresponding to amino acids 492 to 791; the P2A protein of HAV corresponding to amino acids 792 to 980; the P2B protein of HAV corresponding to amino acids 981 to 1087; the P2C protein of HAV corresponding to amino acids 1088 to 1422; the P3A protein of HAV corresponding to amino acids 1423 to 1496; the P3B protein of HAV corresponding to amino acids 1497 to 1519; the P3C protein of HAV corresponding to amino acids 1520 to 1738; and conservative variations thereof, wherein the antigenically reactive HAV peptide is not identical to a HAV polyprotein, wherein the amino acid sequence of at least a first portion of P2A sequence and a second portion of P2A sequence are switched in order with one another relative to the amino acid sequence of wild-type HAV P2 protein and wherein the antigenically reactive peptide binds to an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOS: 38, 42 - 46 [11-72] and conservative variations thereof.